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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/771,536	01/29/2001	William H.R. Langridge	12273-3	9620

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EXAMINER	
HILL, MYRON G	
ART UNIT	**PAPER NUMBER**
1648	12

DATE MAILED: 09/27/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/771,536	LANGRIDGE ET AL.	
	Examiner	Art Unit	
	Myron G. Hill	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the corresp ndence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1- 68* is/are pending in the application.

4a) Of the above claim(s) *1- 49, and 65- 68* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *50- 64* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1- 68* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on 1/25/01 is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *6,7,11* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

This office action is on claims 50- 64.

The Group and/or Art Unit of your application has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Group Art Unit 1648, Examiner Myron Hill.

Election/Restrictions

Restriction to one of the following inventions is required under 35 U.S.C. 121:

I. Claims 1- 21, drawn to a DNA construct, classified in class 536, subclass 23.1.

II. Claims 22- 47, drawn to method of producing an immunogen in a plant, classified in class 435, subclass 410.

III. Claims 50- 64, drawn to a fusion protein, classified in class 435, subclass 69.7.

IV. Claims 48, 49, and 65- 68, drawn to a method of inducing immunity, classified in class 424, subclass 192.1.

The inventions are distinct, each from the other because of the following reasons:

Inventions I and II are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different

product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case the DNA construct could be expressed in E. coli or yeast.

Inventions II and IV are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions are drawn to different methods with different starting materials and different results.

Inventions III and IV are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case the fusion protein could be made from another source.

Because these inventions are distinct for the reasons given above and have acquired a separate status in the art as shown by their different classification, the different search requirements and that the search for one is not coextensive with the search for each of the others, restriction for examination purposes as indicated is proper.

During a telephone conversation with David Farah on 9/9/02 a provisional election was made without traverse to prosecute the invention of Group III, claims 50-64 (call made by A. Chakrabarti). Affirmation of this election must be made by applicant in replying to this Office action. Claims 1- 49 and 65- 68 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 50- 64 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. It is not clear what the term "multimeric" specifies in relation to the cholera toxin subunit. Claims 50- 64 are also rejected under 35 U.S.C. 112, second paragraph, as they are not clear in what is meant by fusion protein because Figure 2 shows a construct that produces 2 fusion proteins. It appears that what is meant could be a protein complex of heterodimers as described on page 17, line 25- page 18, line 8. In claims 53 and 55 it is not clear if "can" intends the inclusion of the second part. If "can" does not include the second cholera toxin, then the claims are rejected for failing to further limit the invention.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 50, 51, 58 and 63 are rejected under 35 U.S.C. 102(b) as being anticipated by Gonzalez et al. (Gene 1993, 133: 227- 232).

Gonzalez teaches a fusion protein that contains a cholera toxin B subunit and a rotavirus antigen (abstract). Gonzalez teaches that peptide antigens are usually ineffective when administered orally but a notable exception is the cholera toxin (A-B_5 where the toxic A moiety is linked to the pentameric B) and this has been used as a carrier/ adjuvant with other antigens and the use of DNA technology to make a fusion protein alleviates the need to couple the polypeptides and reduces downstream processing (page 227 and 228).

Claims 50, 53, 54, and 63 are rejected under 35 U.S.C. 102(b) as being anticipated by Hajishengallis et al. (J. Immunology 1995 vol 154: 4322- 4332).

Hajishengallis teaches a fusion protein that encodes colera toxin A2 and B subunits along with an immunogenic antigen to a mamalian disease (abstract, pages 4322- 4323, 4330 last paragraph and Fig 1).

> (e) the invention was described in-

> (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effect under this subsection of a national application published under section 122(b) only if the international application designating the United States was published under Article 21(2)(a) of such treaty in the English language; or
> (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that a patent shall not be deemed filed in the United States for the purposes of this subsection based on the filing of an international application filed under the treaty defined in section 351(a).

Claims 50, 53, 54, and 63 are rejected under 35 U.S.C. 102(e) as being anticipated by Russell (US 6030624).

Russell teaches a fusion protein that encodes colera toxin A2 and B subunits along with an immunogenic antigen to a mamalian disease(column 10, lines 11- 28).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claim 52 is rejected under 35 U.S.C. 103(a) as being unpatentable over Gonzalez as applied to claims 50, 51, 58 and 63 above, and further in view of Manson et al. (TIBTECH September 1995 vol. 13: 388- 392).

Gonzalez teaches a fusion protein that contains a cholera toxin B subunit and a rotavirus antigen (abstract). Gonzalez teaches that peptide antigens are usually ineffective when administered orally but a notable exception is the cholera toxin ($A\text{-}B_5$

where the toxic A moiety is linked to the pentameric B) and this has been used as a carrier/ adjuvant with other antigens and the use of DNA technology to make a fusion protein alleviates the need to couple the polypeptides and reduces downstream processing (page 227 and 228).

Gonzalez does not teach enterotoxic *E. coli*.

Manson teaches that cholera and enterotoxigentic *E. coli* are important causes of diarrhea and mortality in developing countries, that the enterotoxin from *E. coli* is similar to chorlea toxin in many respects, that both are excellent oral adjuvants that stimulate response to co- fed antigens, both antigens are immunogenic against a mammalian disease, and that they have the adjuvant effect at doses lower than what causes disease (section "E" pages 389- 391).

It would have been obvious to one skilled in the art to express enterotoxic *E. coli* antigens in a fusion protein using the techniques of Gonzalez and the knowledge that the antigen was immunogenic against a mammalian disease. One of skill in the art would have known the advantages of expressing multiple antigens in one source for use as a vaccine and it would have been obvious to combine antigens that would be useful together.

Thus, it would have been *prima facie* obvious to one of ordinary skill in the art to produce a fusion protein that contained a cholera toxin with a reasonable expectation of success.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Myron G. Hill whose telephone number is 703-308-4521. The examiner can normally be reached on 9am-6pm Mon-Fri.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached on 703-308-4247. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4242 for regular communications and 703-308-4242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Myron G. Hill
Patent Examiner
September 24, 2002

MARY E. MOSHER
PRIMARY EXAMINER
GROUP ~~1800~~ 1600